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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,445	03/09/2001	Gary Van Nest	377882001300	7011

25226 7590 06/14/2004

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,445	NEST ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,9-12,14 and 23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,9-12,14 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Currently, claims 1-4, 6, 9-12, 14, and 23-26 are pending and under consideration. Claims 1-4, 6, 9-12, 14, and 23-26 were pending and rejected in the prior action, mailed on December 2, 2003. That action was made Final. The Applicant filed an amendment on February 13, 2004 to amend claims 1, 6, 9, and 14. The amendment was not entered into the Application.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2004 (the Response) has been entered.

3. The Art Unit location of your application, and the examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. **(New Rejection)** Claims 1-4, 6, 9-12, 14, and 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods of delaying the development, or reducing the severity, of a symptom of papillomavirus infection through administration of an immunostimulatory DNA sequence (ISS) to papillomavirus-associated lesion. It is unclear from the claims if the claimed invention is directed to the treatment of any symptom of papillomavirus infection, or is limited to the treatment of the lesions associated with the infection. It is suggested that the claims be amended such that they read on methods of delaying the development of, or reducing the severity of, a papillomavirus-associated lesion. Clarification is required.

6. **(New Rejection)** Claims 1-4, 6, 23, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been amended to read on methods of delaying the development of a symptom of papillomavirus-infection in a mammal through administration of an ISS at a papillomavirus-associated lesion. However, the Applicant has not disclosed what other symptoms may be treated other than the lesions themselves. In view of this, and because the claims are drawn to methods of delaying the development of those lesions, it is unclear how the ISS can both delay the development of the lesion and be administered to the site of the lesion. This is because the ISS cannot be administered to the site of the lesion if it has not yet been formed. Clarification is required.

Because the claim requires the presence of the lesion in order for the method to be performed, the claims will be treated, unless otherwise indicated, as including methods of reducing the severity of such lesions.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(Prior Rejection- Maintained in part)** Claims 1-4, 6, 9-12, and 23-26 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of reducing the severity of a papillomavirus associated lesion when administered to the site of a lesion, does not reasonably provide enablement for methods of delaying the development of lesions through administration prior to the development of the lesion, or for methods wherein the ISS is administered to regions outside of the affected area. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant has amended the claims such that they now require that the ISS is administered at the site of the lesion. In view of this amendment, the portion of the rejection relating to the site of administration is withdrawn.

The rejection is also withdrawn as to claims 9-12, 25, and 26. This is because the Applicant has demonstrated that the administration of the ISS results in a regression of the

tumor. Such a regression would appear to constitute a regression of the severity of the lesion. Thus, the Applicant is enabled for methods of reducing the severity of the lesion.

The rejection is maintained however with respect to claims 1-4, 6, 23, and 24. These claims were rejected as lacking enablement because the Applicant has not established that the administration of an ISS would be effective in delaying the development of lesion in a mammal. For the purposes of this rejection, it is assumed that the claims still read on methods of administering the ISS prior to the onset of the lesion formation. Because, as was described in the prior actions, the Applicant has not provided an enabling disclosure for such a method, the rejection is maintained against these claims for the reasons of record.

9. **(New Rejection)** Claims 1-4, 6, 9-12, 14, and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been described above. As was indicated above, the claims appear to be drawn to the treatment of any symptom of a papillomavirus infection through administration of an ISS in the absence of a viral antigen, to a papillomavirus-associated lesion. However, while the Applicant has demonstrated that the administration of an ISS may reduce the severity of a papillomavirus-associated lesion, the Applicant has not demonstrated that such treatment would have any effect on other symptoms of the viral infection.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the claims are drawn to methods of treating any symptom of papillomavirus infection. However, the only types of symptoms identified by the Applicant are those involving the formation of lesions. The Applicant has neither provided examples of other types of symptoms, or provided any indication that such other symptoms may be treated by the administration of an ISS as described in the claims. Because the Applicant has not provided written description support for the treatment of any symptom of papillomavirus infection other than papillomavirus-associated lesions, the Applicant has not provided sufficient written description support for the full scope of the claimed methods.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **(New Rejection)** Claims 1-3, 6, 9-11, and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Beutner et al. (J Am Acad Dermatol 38(2/1): 230-39) and Bauman et al. (Pediatr Clin N Am 43(6): 1385-401), and further in view of the teachings of Yamamoto et al., (Jpn J Cancer Res 85: 775-79- of record in the IDS of February 2002). The claims read on methods of treating papillomavirus-associated lesions through administration of an indicated ISS to the lesion.

Each of Beutner and Bauman teach that one means for the treatment of papillomavirus-associated lesions is through adjuvant therapy. In particular, Bauman teaches that regression of the lesions may be achieved through administration of interferon-alpha to the lesions. See, pages 1393-94. Further, Beutner teaches that similar results may also be achieved through administration of other adjuvants. Abstract. However, this reference indicates that the efficacy of the adjuvant used therein may be due, at least in part, to the induction of interferon-alpha. Page 237. In view of these teachings, it would have been obvious to those in the art that to use adjuvants which induce interferon-alpha production for the treatment of warts or other papillomavirus-associated lesions. There would have been a reasonable expectation in the use of such adjuvants due to the teachings of these two references, which illustrate the efficacy of both IFA-α, and an adjuvant which induces its production, for the treatment of such lesions.

However, neither of these references teaches or suggests the use of an ISS as the adjuvant. Yamamoto teaches that an immunostimulatory sequence comprising the sequence AACGTTCG was a strong inducer of IFN-α. Pages 776-77. See also, Yamamoto et al., J Immunol 148(12): 4072-76, at 4075; and Ballas et al., J Immunol 157: 1840-45, at 1843 (both of record in the Feb 2002 IDS, and each indicating that sequences comprising the oligomer AACGTT are effective for the induction of IFN-α). Because the adjuvant of Yamamoto is disclosed in the art as capable of inducing IFN-α production, and because the art indicates that adjuvants with this activity may be used for the treatment of papillomavirus-associated lesions, it would have been obvious to those in the art to use the oligonucleotide adjuvants of Yamamoto in such a method. There would have been a reasonable expectation of success in the use due to the teachings regarding IFN-α induction in Beutner and Bauman, and the fact that the Yamamoto adjuvant was known to be able to induce this cytokine. The cumulative teachings of these references therefore render the claimed invention obvious.

12. **(New Rejection)** Claims 4 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beutner, Bauman, and Yamamoto as applied to claims 1-3, 6, 9-11, and 23-26 above, and further in view of either of Raz et al. (U.S. patent 6,514,948), or Schwartz et al. (WO 98/55495- of record in the Feb 2002 IDS). Claims 4 and 12 further limit the methods of the previously described claims to embodiments wherein the ISS comprises SEQ ID NO: 1. The teachings of each of Beutner, Bauman, and Yamamoto have been described above. These references do not, alone, teach or suggest the use of SEQ ID NO: 1 in a method for the treatment of papillomavirus-associated lesions.

Each of Raz and Schwartz teach an ISS with the sequence of SEQ ID NO: 1. See e.g., Raz, col 10, and Schwartz, page 29. Each of these sequences comprise a sequence taught in the Yamamoto reference to induce IFN-α production as part of its adjuvant activity. Cf., Raz, col 10, and Schwartz, page 29; with Yamamoto, page 777 (each of the sequences comprising the palindrome AACGTT). Further, each of Schwartz and Raz indicate that it is the presence of the shorter sequence that allows for the ISS activity. See e.g., Raz, columns 7-8, and claims 1; and Schwartz, page 7. In view of the these teachings indicating that SEQ ID NO: 1 is an effective ISS, and the teachings regarding the IFN-α inducing activity of the smaller sequences described above, it would have been obvious for those in the art to use the ISS of SEQ ID NO: 1 as the adjuvant for the methods suggested by the combination of Beutner, Bauman, and Yamamoto. Because the art teaches that SEQ ID NO: 1 is an effective ISS, and because the art teaches that the palindrome sequence found within SEQ ID NO: 1 is effective for the production of IFN-α, there would have been a reasonable expectation of success in the combination of the references. The cumulative teachings of these references therefore render the claimed invention obvious.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 6/13/04
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